PATENT COOPERATION TREAT

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INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY
(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference P05980PC00	FOR FURTHER ACTION See Form PCT/IPEA/416	
International application No. PCT/SE2003/001652	International filing date *(day/month/year)* 24.10.2003	Priority date *(day/month/year)* 24.10.2002
International Patent Classification (IPC) or national classification and IPC A61K 38/44, G01N 33/574		
Applicant Karolinska Innovations AB et al		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 6 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *(sent to the applicant and to the International Bureau)* a total of 2 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s))
      _____, containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).
4. This report contains indications relating to the following items:
   - ☒ Box No. I Basis of the report
   - ☐ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12.05.2004	14.01.2005
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Form PCT/IPEA/409 (cover sheet) (January 2004)

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE2003/001652

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ This report is based on a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of:

- ☐ international search (under Rules 12.3 and 23.1(b))
- ☐ publication of the international application (under Rule 12.4)
- ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report):*

☐ the international application as originally filed/furnished

☒ the description:

pages 1-17 as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☒ the claims:

pages _____ as originally filed/furnished
pages* _____ as amended (together with any statement) under Article 19
pages* 1-2 received by this Authority on 11.01.2005
pages* _____ received by this Authority on _____

☒ the drawings:

pages 1-7 as originally filed/furnished
pages* _____ received by this Authority on _____
pages* _____ received by this Authority on _____

☒ a sequence listing and/or any related table(s) – see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to the sequence listing *(specify)*: _____

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).

- ☐ the description, pages _____
- ☐ the claims, Nos. _____
- ☐ the drawings, sheets/figs _____
- ☐ the sequence listing *(specify)*: _____
- ☐ any table(s) related to the sequence listing *(specify)*: _____

* *If item 4 applies, some or all of those sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

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Supplemental Box Relating to Sequence Listing

Continuation of Box No. I, item 2:

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this report was established on the basis of:

   a. type of material

   ☒ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material

   ☒ in written format

   ☐ in computer readable form

   c. time of filing/furnishing

   ☒ contained in the international application as filed

   ☐ filed together with the international application in computer readable form

   ☐ furnished subsequently to this Authority for the purposes of search and/or examination

   ☐ received by this Authority as an amendment* on _____

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

* *If item 4 in Box No. I applies, the listing and/or table(s) related thereto, which form part of the basis of the report, may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 4, 7

because:

☒ the said international application, or the said claims Nos. 4, 7 relate to the following subject matter which does not require an international preliminary examination *(specify)*:

See PCT Rule 67.1.(iv).: Methods for treatment of the human or animal body by surgery or therapy, as well as diagnostic methods.

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for said claims Nos. _____

☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form
- ☐ has not been furnished
- ☐ does not comply with the standard

the computer readable form
- ☐ has not been furnished
- ☐ does not comply with the standard

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in the Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/SE2003/001652

Box No. V **Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

Novelty (N)	Claims	1-3,5-6,8-10	YES
	Claims		NO
Inventive step (IS)	Claims	1-3,5-6,8-10	YES
	Claims		NO
Industrial applicability (IA)	Claims	1-3,5-6,8-10	YES
	Claims		NO

2. Citations and explanations (Rule 70.7)

Reference is made to the following documents:

D1 EMBL databas, acession nr Q8TAV3, Strausberg, R., 1 juni 2002.
D2: Jounaidi et al, Cancer Research, 61(11) page 4437
D3: STN database, CAPLUS, VOL 126, Oyama et al, Anticancer Research, 1997, 17(1B), pages 583-587
D4: WO 01/58455 (see claim 29)
D5: STN database, CAPLUS, vol 125, Vasquez et al, International Journal of Oncology, 1996, 9(3), pages 427-431, abstract nr 292401
D6: Biosis database, accession nr PREV200200495945, Itoga et al., Alcoholism Clinical and Experimental Research, Aug 2002, vol 26, pages 15s-19s.

The claimed invention relates to the use of the cytochrome P450 enzyme CYP2W1 and its promoter as a drug target in both screening for therapeutic agents and in cancer therapy. The invention is based on the discovery that CYP2W1 was found to be selectively expressed in tumour tissues and especially in lung carcinoma, colon carcinoma and ovarian carcinoma.

An enzyme isolated from human lung tissue and belonging to the cytochrome P450 family has been disclosed in D1. It has a length of 434 amino acids and has 100% identity in these 434 amino acids. It has been isolated from lung tissue but it has not been shown to be involved with cancer.

The claimed enzyme differs from the known enzyme in that it has 490 amino acids instead of 434.

.../...

Supplemental Box

In case the space in any of the preceding boxes is not sufficient.
Continuation of: Box V

The problem to be solved by claims 1-3, 5-6 and 8-10 is to prepare an alternative drug and therapy for cancer especially lung carcinoma, colon carcinoma and ovarian carcinoma.

The solution to this problem is to use CYP2W1 having SEQ ID NO:2.

Documents D2,D3,D4,D5 and D6 all disclose different cytochrome P450 enzymes belonging to CYP2 family and their existence in cancer cells. It is known from these documents that these enzymes exist in cancer cells and that they can be used in cancer therapy for treating, for example, lung carcinoma, colon carcinoma and ovarian carcinoma.

These cytochrome P450 enzymes are however not selectively expressed in tumour tissues but are also expressed in normal tissues.

Therefore it is not considered obvious that the claimed cytochrome P450 enzyme belonging to family 2 and subfamily W1 and having the sequence SEQ ID NO:2 would be only expressed in tumour tissue and thus especially useful for cancer therapy.

Consequently, the subject-matter in claims 1-3, 5-6 and 8-10 is novel and considered to involve an inventive step.

CLAIMS

1. A compound comprising one part conferring cytotoxic and/or anti-cancer effects to the compound and one part conferring specific binding affinity towards a CYP2W1-molecule according to SEQ ID No: 8 to the compound.

2. A pharmaceutical composition comprising a compound according to claim 1 and pharmaceutically acceptable excipients and/or carriers.

3. An antibody, preferably a monoclonal antibody, binding specifically to CYP2W1.

4. Use of the cytochrome P450 enzyme CYP2W1 and genetic variants thereof as a drug target in cancer therapy, preferably in the treatment of lung tumours, colon tumours and/or ovarian tumours.

5. A method of providing therapeutic agents for cancer therapy, comprising screening for such agents by using CYP2W1 as a drug target.

6. A method according to claim 5, comprising screening for therapeutic agents modulating, preferably increasing, the activity of CYP2W1.

7. A method of treating cancer, comprising administering to a subject in need thereof a therapeutically effective amount of a substance activated by the enzyme CYP2W1 and/or inducing the enzyme CYP2W1 and/or the compound according to claim 1.

8. DNA-molecule with nucleotide sequence according to SEQ ID NO: 10.

9. Use of a DNA-molecule according to claim 8 in the manufacture of a medicament.

10. A method of providing therapeutic agents for cancer therapy, comprising screening for such agents modulating expression of genes regulated by the CYP2W1 promoter according to SEQ ID NO: 10.